Drug Calculations in Alzheimer's Disease and Anxiety

Acetylcholinesterase inhibitors are recommended by the National Institute for Health and Care Excellence (NICE, 2011) for the use of for people with mild to moderate Alzheimer's Disease. Memantine is recommended for those with either mild to moderate Alzheimer's Disease who cannot tolerate acetylcholinesterase inhibitors or in severe Alzheimer's disease. NICE uses the mini mental state examination (MMSE) to class the severity of Alzheimer's Disease.

A patient is taking donepezil 10mg daily and due to a deterioration in day to day functioning and reduction in the MMSE score, it is decided to start memantine. The dose of memantine is initially is 5mg daily, increased in steps of 5 mg at weekly intervals to a maximum of 20 mg daily. The tablets are available in 5mg, 10mg, 15mg and 20mg.

(a) How many days and tablets will it take to reach a full week of the dose of 20mg daily?

After a year the patient is admitted into hospital with behavioural and psychological symptoms of dementia. The patient is currently taking memantine 20mg daily and citalopram 20mg daily and is refusing to take medication. It is decided to administer medication covertly in the patients' best interest. The medicines are converted to oral liquid formulation for it to be given in fluids.

Memantine oral solution is available as a pump device (10mg/mL) and available as a 50mL pump delivering 5mg per actuation.

(b) How many actuations of memantine would be required have occurred during 28 days of patients' current dose?
(c) How many mL of is delivered per actuation?
(d) How many days will a 50mL pump last?

Citalopram hydrochloride liquid is available as drops (40mg/mL). 4 drops is 8mg citalopram hydrochloride which is equivalent to 10mg citalopram hydrobromide tablets.

(e) How many drops are required per dose?
(f) How many mL will be delivered?
(g) How many days will a 15mL bottle last?

During the inpatient stay, diazepam was utilised on a regular basis for anxiety. This was gradually reduced and stopped when the patient became more settled. Benzodiazepines should only be used on a short term basis because long term use is associated with dependence, becoming ineffective and other adverse effects (Joint Formulary Committee, 2015; Ferguson, 2012).

Abrupt discontinuation of long term benzodiazepine use can lead to severe withdrawal symptoms (Joint Formulary Committee, 2014).The British National Formulary (BNF) goes on to state when withdrawing a patient from a benzodiazepine it is recommended to switch them to an equivalent dose of diazepam, if not already on so, and to reduce gradually.

Convert the following to diazepam in the table below:

Currently prescribed in 24hrs	BNF approximate equivalence dose to 5mg	How much diazepam

	diazepam (Joint Formulary Committee, 2015)	required in 24hrs
Temazepam 40 mg	Temazepam 10 mg	(h)
Clonazepam 2mg	Clonazepam 250 micrograms	(i)
Clobazam 10 mg	Clobazam 10 mg	(j)
Chlordiazepoxide 25mg	Chlordiazepoxide 12.5 mg	(k)
Lorazepam 3mg	Lorazepam 500 micrograms	(l)
Nitrazepam 2.5 mg	Nitrazepam 5 mg	(m)
Oxazepam 35 mg	Oxazepam 10 mg	(n)

References

Ferguson B (2012), Benzodiazepines: guide to withdrawing in general practice, Prescriber, vol 23, no 7, p35-39

Joint Formulary Committee (2014) British National Formulary, 68th edition, London: BMJ Group and Pharmaceutical Press

National Institute for Health and Care Excellence (2011), Donepezil, galantamine, rivastigmine and memantine for the treatment of Alzheimer's disease : TA217, London: National Institute for Health and Care Excellence, available at http://www.nice.org.uk/guidance/TA217 (last accessed 04/05/15)

Answers

(a) Week 1: 5mg daily
Week 2: 10 mg daily

Week 3: 15mg daily
Week 4: 20mg daily

28 days to reach full week of 20mg daily
28 tablets required in total

(b) Current dose 20mg daily
5mg is delivered per actuation and therefore (20mg /5mg) 4 actuations daily are required
28 days x 4 actuations: 112 actuations

(c) Oral solution is 10mg/mL and each actuation delivers 5mg. Therefore divide 10mg/1mL by 2
Each actuation delivers 5mg/0.5mLs

(d) 4 actuations delivers (0.5ml x 4) 2mL and therefore 50mL bottle will last (50mL /2mL) 25 days

(e) 10mg citalopram hydrobromide tablets = 4 drops (8mg citalopram hydrochloride liquid)
Therefore
20mg tablets = 2 x 4 drops (2x 8mg liquid)
8 drops required (16mg liquid)

(f) From previous question 16mg liquid is required
Using proportional sets

1mL/40mg = y/ 16mg
(1 x 16mg)/40mg = y
y = 0.4mL

(g) Citalopram bottle contains 15mL
Previous question determined that 0.4mL dose required
Therefore 0.4mL will last (15mL/0.4mL) 37 whole days

(h) Temazepam 10mg is equivalent to diazepam 5mg
Temazepam 10mg x 4 = temazepam 40mg
Therefore temazepam 40mg is equivalent to (4 x 5) diazepam 20mg

(i) Clonazepam 250 micrograms is equivalent to 5mg diazepam.
Clonazepam 250 micrograms x 8 = clonazepam 2000 microgram (2mg)
Therefore 2mg clonazepam is equivalent to (8 x 5) diazepam 40mg

(j) Clobazam 10mg equivalent to 5mg diazepam.
Therefore clobazam 10mg is equivalent to diazepam 5mg

(k) Chlordiazepoxide 12.5 mg is equivalent to 5mg diazepam.
Chlordiazepoxide 12.5 mg x 2 = Chlordiazepoxide 25mg.
Therefore chlordiazepoxide 25mg is equivalent to (2 x 5) diazepam 10mg

(l) Lorazepam 500 micrograms is equivalent to 5mg diazepam.
Lorazepam 500 micrograms x 6 = Lorazepam
3000 micrograms (3mg)
Therefore lorazepam 3mg is equivalent (6 x 5) diazepam 30mg

(m) Nitrazepam 5mg equivalent to 5mg diazepam.
Diazepam equivalent is equal that of nitrazepam.

Therefore Nitrazepam 2.5mg is equivalent diazepam 2.5mg.

(n) Oxazepam 10mg equivalent to 5mg diazepam.
Diazepam equivalent is half that of oxazepam.
Therefore oxazepam 35 mg is equivalent (35/2) diazepam 17.5mg.